

# Non-AIDS Defining Malignancies: A Clinical Update

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# Disclosures

No conflicts of interests or disclosures to report

# Objectives

- **Describe the epidemiology of non AIDS defining malignancies**
- **Characterize treatment factors which affect outcomes among HIV infected patients**
- **Cancer prevention**

# MMWR

## Epidemiologic Notes and Reports

- 305 Kaposi's Sarcoma and *Pneumocystis* Pneumonia Among Homosexual Men — New York City and California  
 308 Cutaneous Larva Migrans in American Tourists — Martinique and Mexico  
 314 Measles — U.S. Military

## MORBIDITY AND MORTALITY WEEKLY REPORT

### *Epidemiologic Notes and Reports*

#### Kaposi's Sarcoma and *Pneumocystis* Pneumonia Among Homosexual Men — New York City and California

During the past 30 months, Kaposi's sarcoma (KS), an uncommonly reported malignancy in the United States, has been diagnosed in 26 homosexual men (20 in New York City [NYC]; 6 in California). The 26 patients range in age from 26-51 years (mean 39 years). Eight of these patients died (7 in NYC, 1 in California)—all 8 within 24 months after KS was diagnosed. The diagnoses in all 26 cases were based on histopathological examination of skin lesions, lymph nodes, or tumor in other organs. Twenty-five of the 26 patients were white, 1 was black. Presenting complaints from 20 of these patients are shown in Table 1.

Skin or mucous membrane lesions, often dark blue to violaceous plaques or nodules, were present in most of the patients on their initial physician visit. However, these lesions were not always present and often were considered benign by the patient and his physician.

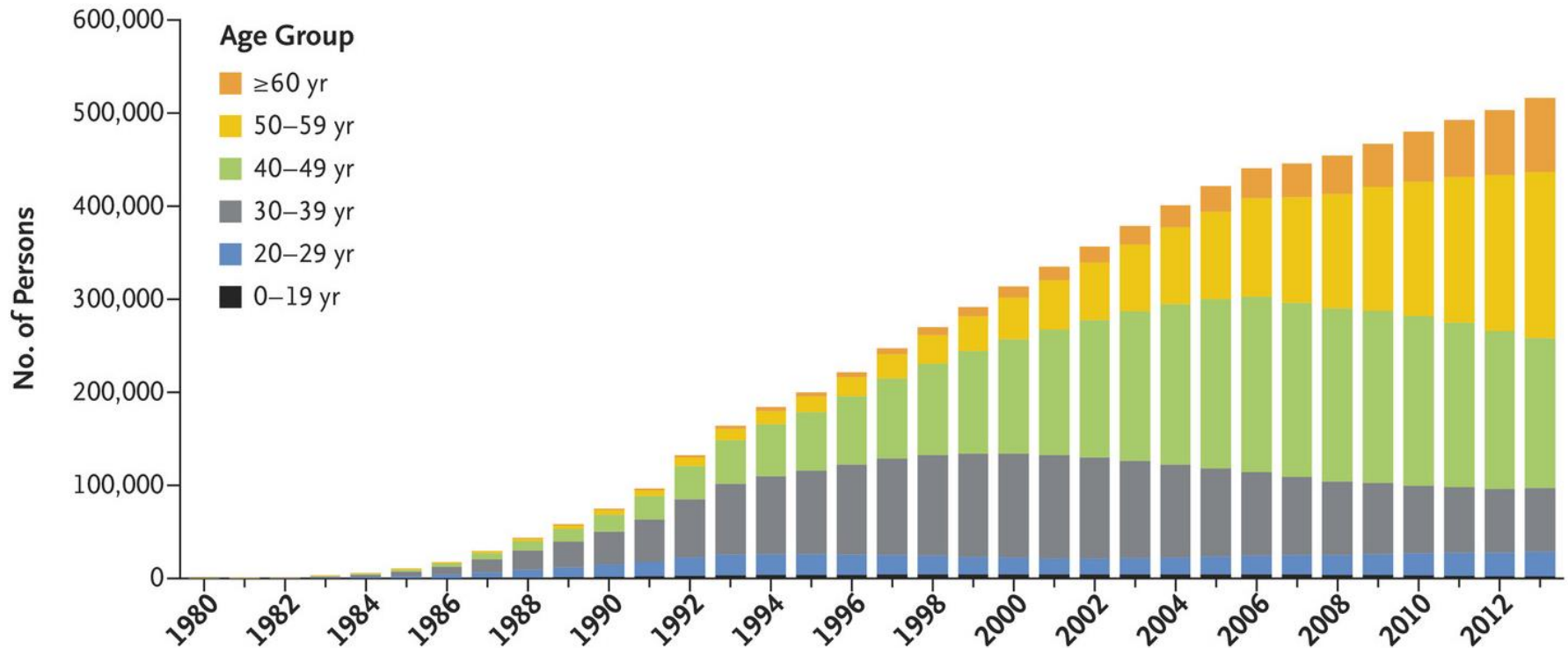
A review of the New York University Coordinated Cancer Registry for KS in men under age 50 revealed no cases from 1970-1979 at Bellevue Hospital and 3 cases in this age group at the New York University Hospital from 1961-1979.

Seven KS patients had serious infections diagnosed after their initial physician visit. Six patients had pneumonia (4 biopsy confirmed as due to *Pneumocystis carinii* [PC]), and one had necrotizing toxoplasmosis of the central nervous system. One of the patients with *Pneumocystis* pneumonia also experienced severe, recurrent, herpes simplex infection; extensive candidiasis; and cryptococcal meningitis. The results of tests for cytomegalovirus (CMV) infection were available for 12 patients. All 12 had serological evidence of past or present CMV infection. In 3 patients for whom culture results were available, CMV was isolated from blood, urine and/or lung of all 3. Past infections with amebiasis and hepatitis were commonly reported.

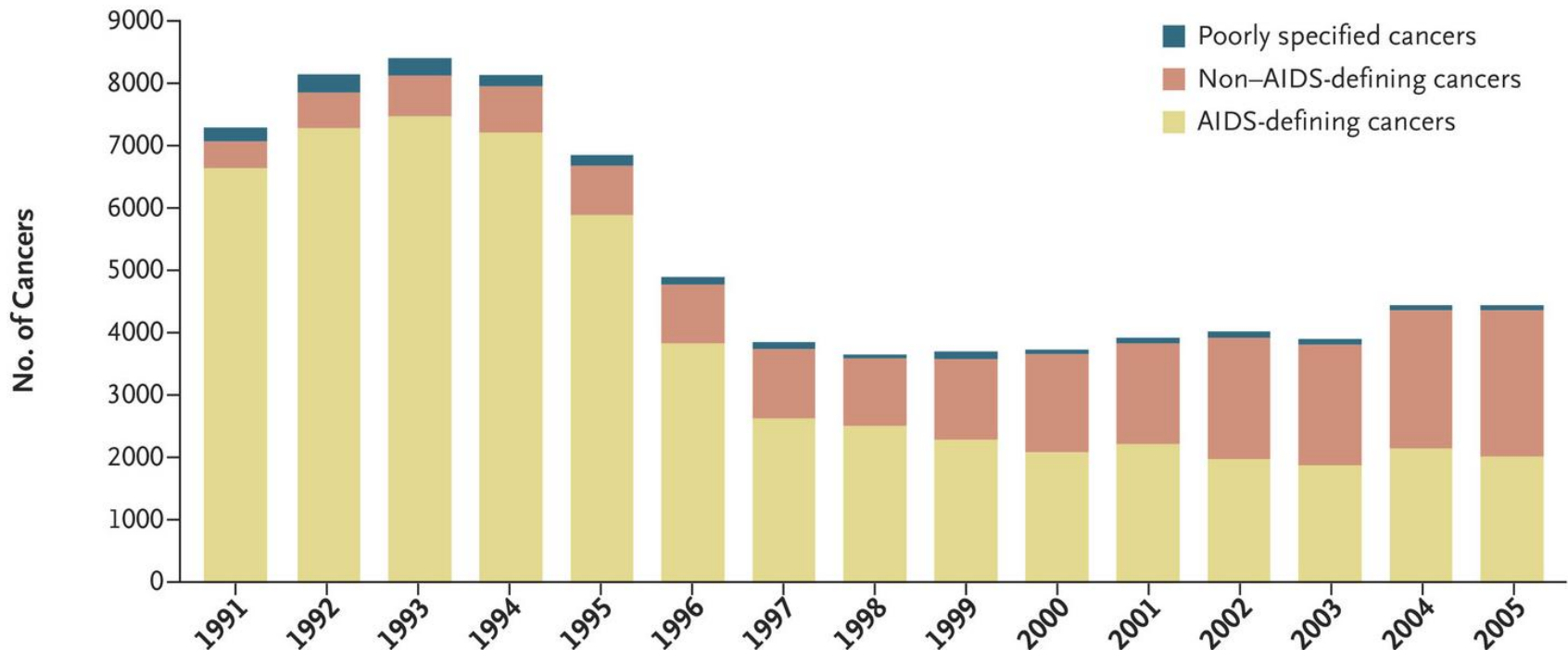
TABLE 1. Presenting complaints in 20 patients with Kaposi's sarcoma

Presenting complaint	Number (percentage) of patients
Skin lesion(s) only	10 (50%)
Skin lesions plus lymphadenopathy	4 (20%)
Oral mucosal lesion only	1 (5%)
Inguinal adenopathy plus perirectal abscess	1 (5%)
Weight loss and fever	2 (10%)
Weight loss, fever, and pneumonia (one due to <i>Pneumocystis carinii</i> )	2 (10%)

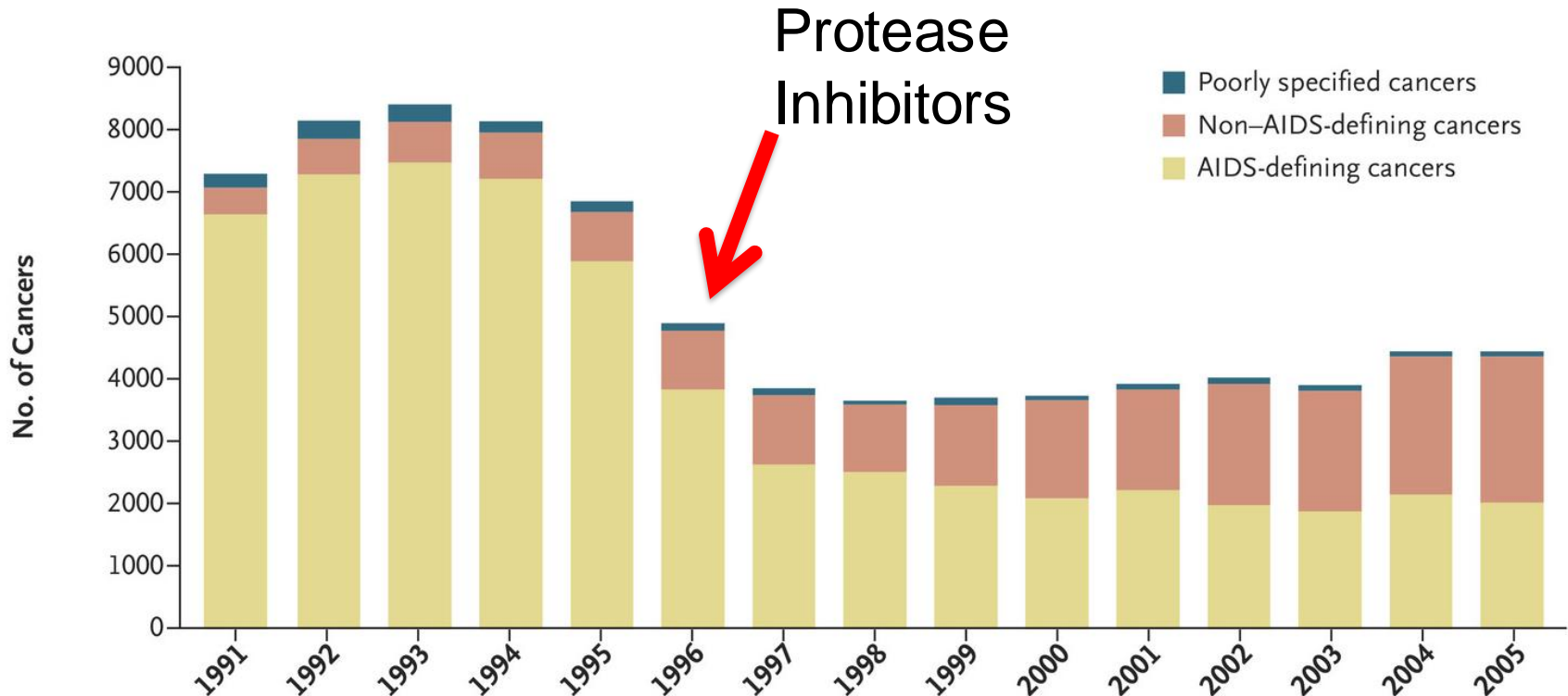
# Persons with AIDS



# Cancers Among Persons with AIDS



# Cancers Among Persons with AIDS

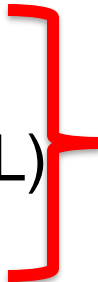



# HIV and Cancer

- Up to 3000x greater risk
- Leading cause of death
- Estimated 8,000 cases annually
  - ~50% increase over the expected number in the general population



# HIV and Cancer

- AIDS-defining cancers
  - Kaposi Sarcoma
  - Non-Hodgkin lymphoma (NHL)
  - Cervical cancer

Associated with another cancer-causing virus
- Non-AIDS defining cancers
  - Anal cancer
  - Liver cancer
  - Hodgkin lymphoma
  - Lung cancer

Associated with another cancer-causing virus

# HIV and Cancer

- AIDS-defining cancers
  - Kaposi Sarcoma
  - non-Hodgkin lymphoma (NHL)
  - cervical cancer

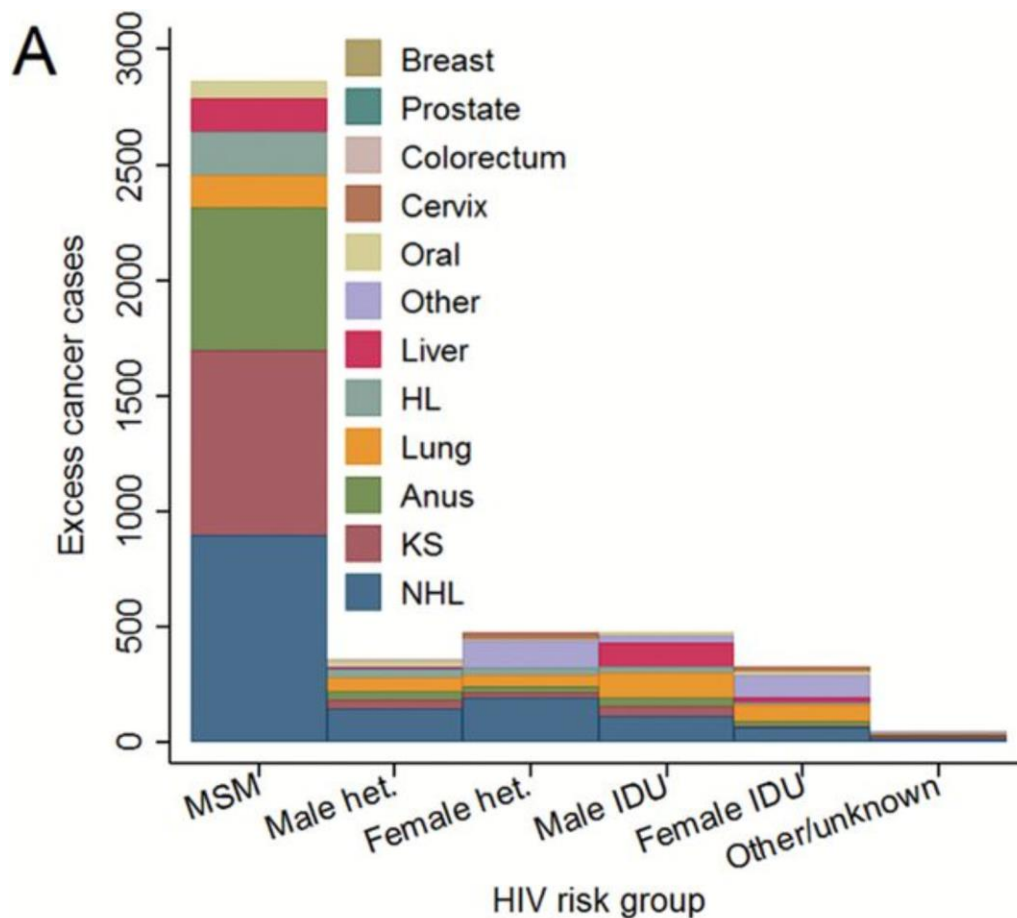
} More common soon after diagnosis
- Non-AIDS defining cancers
  - Anal cancer
  - Liver cancer
  - Hodgkin lymphoma
  - Lung cancer

} More common 5+ years after diagnosis

# Common Malignancies in HIV-infected Patients

Malignancy	Standard Incidence Ratio (HIV only / AIDS)	Estimated % of all cancers in HIV 2010	Estimated US Cases in HIV+ 2010
<b><i>AIDS-Defining Malignancies</i></b>			
<b>Non-Hodgkin lymphoma</b>			
Systemic	10-15 / 30-60	19%	1493
Primary CNS lymphoma	250 / 1,020	2%	157
Kaposi sarcoma	1,300 / 3,640	12%	910
Cervical cancer	2.9 / 5.3	1%	80
<b><i>Non-AIDS Defining Malignancies</i></b>			
Lung cancer	2.6 / 2.6	11%	840
Anal cancer	9.2 / 20	10%	760
Hepatocellular carcinoma	2.7 / 3.3	5%	390
Classical Hodgkin lymphoma	5.6 / 14	4%	320
Oropharyngeal	1.7 / 2.1	4%	280
<b>TOTAL</b>		<b>68%</b>	<b>5230</b>

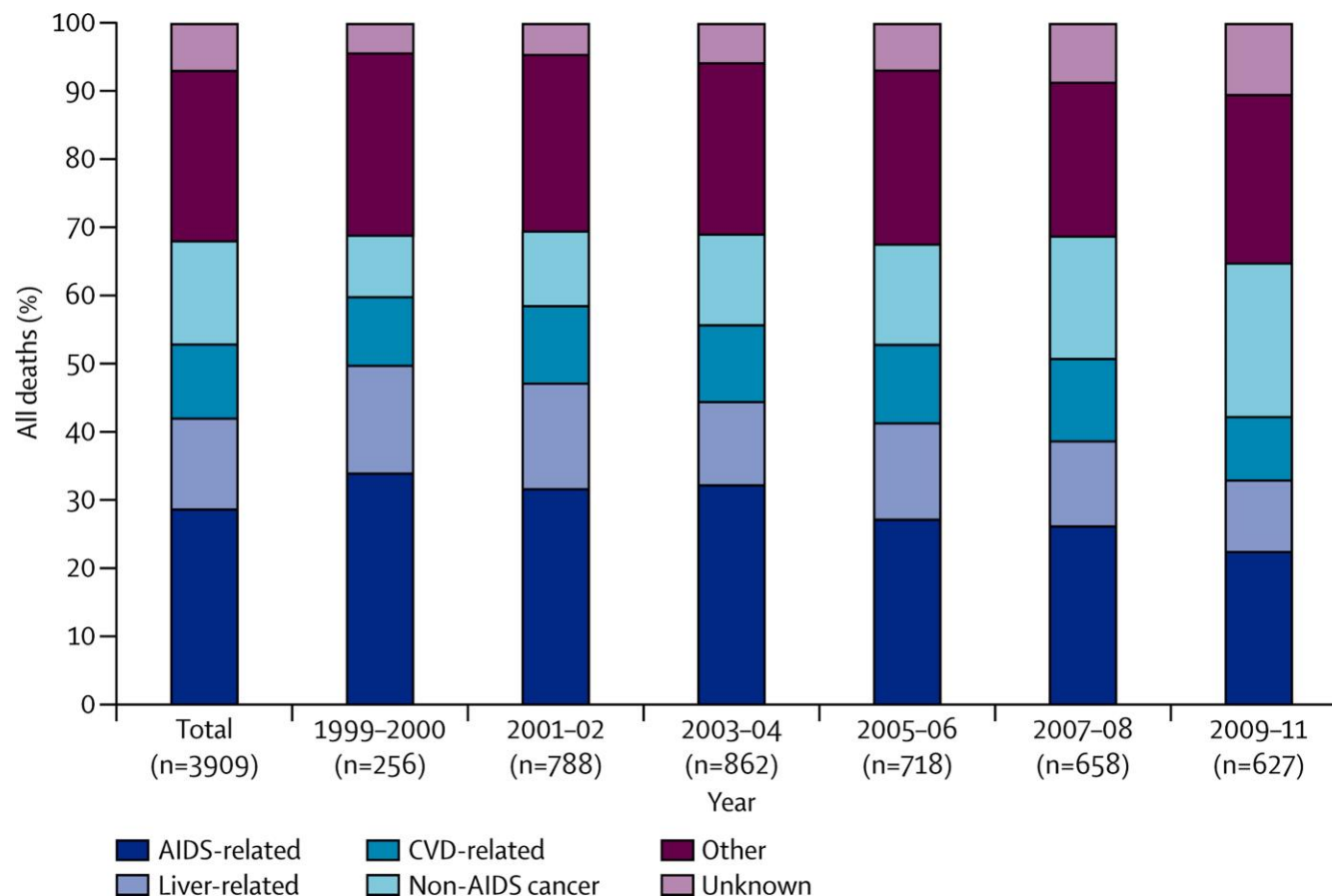
# Excess Cancer Burden Among HIV-Infected Population, US.



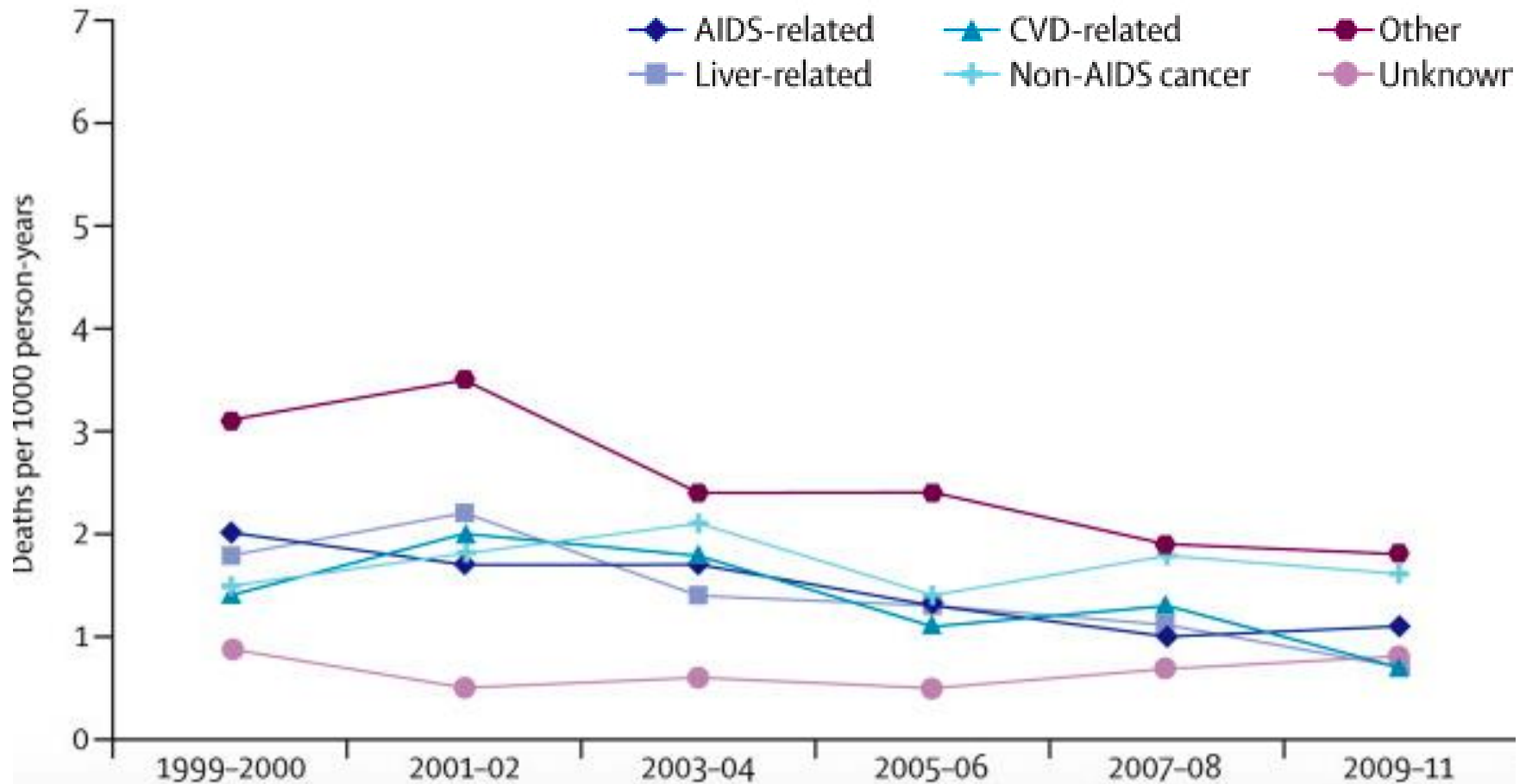
# Factors Associated with Increased Incidence

- Immune dysregulation
  - Impaired immunologic control of oncogenic viruses
  - Immune exhaustion
- Chronic antigenic stimulation
- Cytokine dysregulation
- Proliferative signaling (e.g. angiogenesis)
- Smoking prevalence

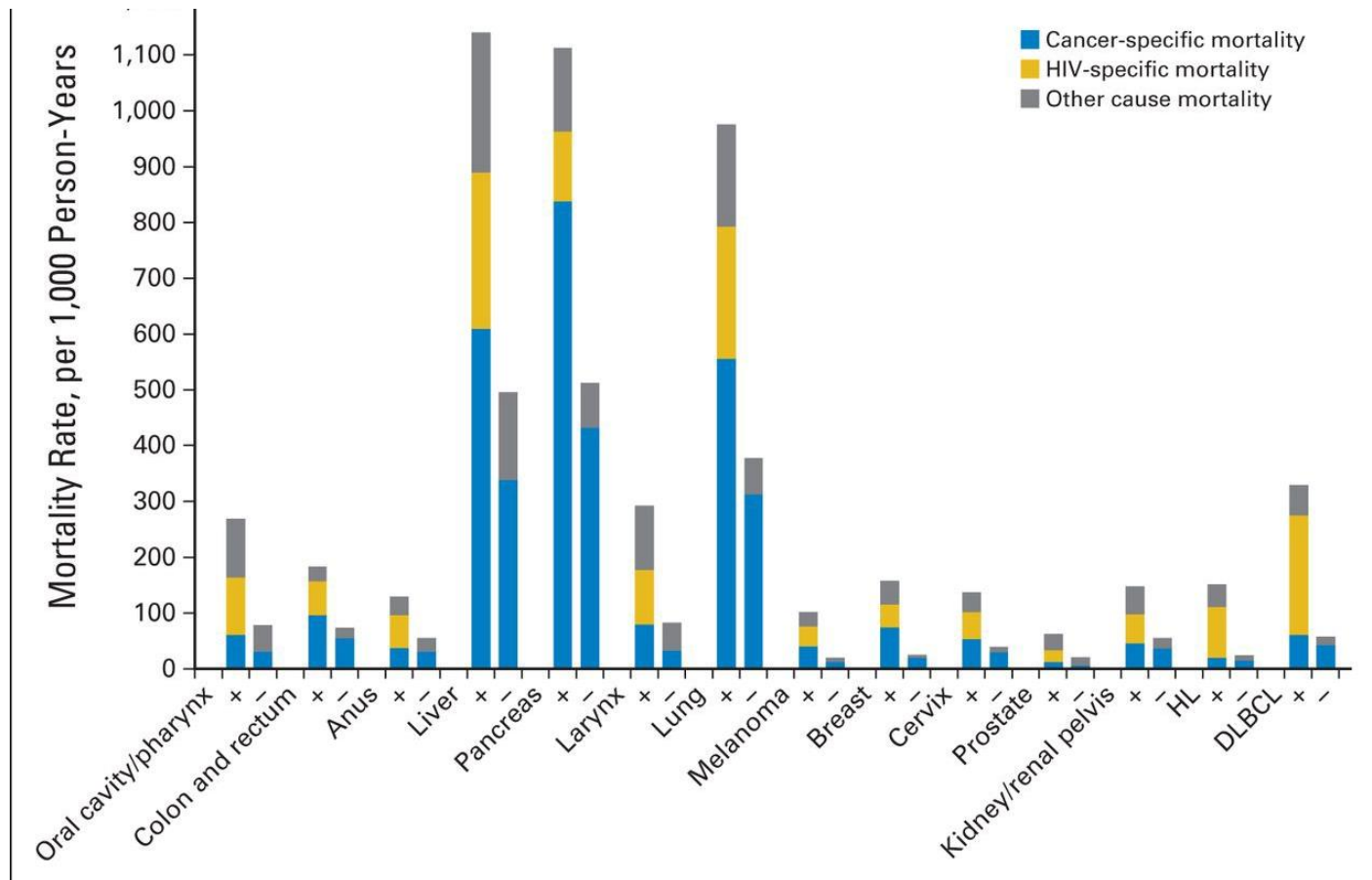
# Causes of Death Among Patients with HIV



# Causes of Death Among Patients with HIV (viral load < 400 copies/mL)



# Age-standardized mortality rates in HIV-infected and HIV-uninfected patients with cancer





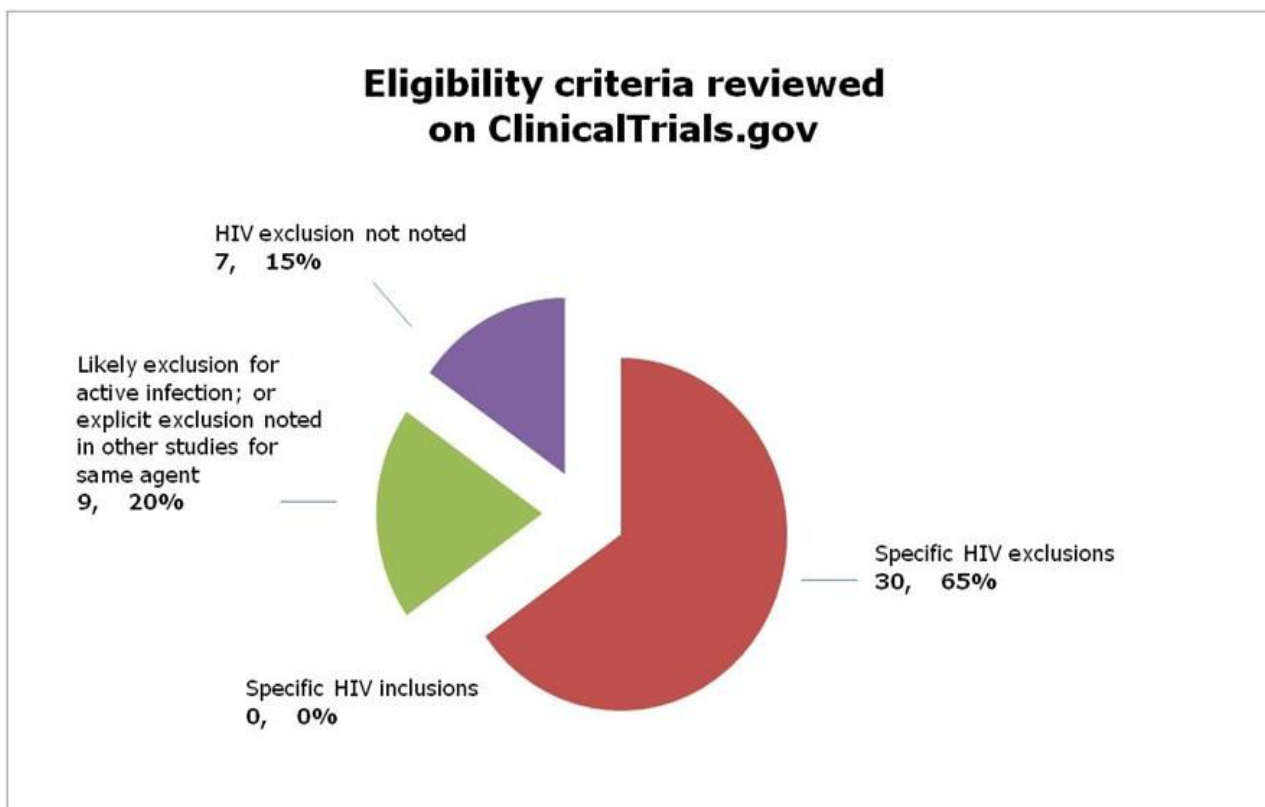
# Disparities in Care

- HIV-infected patients with cancer have higher mortality compared to HIV-uninfected patients
  - Delayed diagnoses
  - Advanced stage
  - Immunosuppression (and AIDS-related complications)
  - Lack of appropriate treatment
    - Independent of insurance status and comorbidities

# Provider Concerns

- Exclusion from clinical trials
  - Limiting generalizability
- Lack of cancer treatment guidelines
- Concerns about ART co-administration

# Current HIV-Related Eligibility Criteria for 46 New Drug Applications



## Modernizing Clinical Trial Eligibility Criteria: Recommendations of the American Society of Clinical Oncology–Friends of Cancer Research HIV Working Group

*Thomas S. Uldrick, Gwynn Ison, Michelle A. Rudek, Ariela Noy, Karl Schwartz, Suanna Bruinooge, Caroline Schenkel, Barry Miller, Kieron Dunleavy, Judy Wang, Jerome Zeldis, and Richard F. Little*



**NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)**

# **Cancer in People Living with HIV**

Version 1.2018 — February 27, 2018

**NCCN.org**



# Anal Cancer

- Incidence rising
- Risk factors: HIV, HPV, smoking, MSM
- 97% of anal cancer in PLWH were in excess
- 83% of excess cases occurred among men who have sex with men
- 71% among those living five or more years since AIDS onset.

# Anal Cancer

- Develop from precursor lesion
  - AIN1 - low grade squamous intraepithelial lesion
  - AIN 2, 3 - high grade squamous intraepithelial lesion
- Histology: typically squamous cell
- Treatment: 5-fluorouracil plus mitomycin chemotherapy with radiation

# ANCHOR: Anal Cancer HSIL Outcomes Research Study (HMC, VM, Polyclinic)

Purpose: Does treatment of anal HSIL (pre-cancerous cells) prevent the development of anal cancer

- Multicenter, phase III randomized trial
- Planned study of 5085 HIV+ men and women with anal HSIL
- Patients with HSIL (pre-cancer) are randomized:
  - 1) Active monitoring (no treatment of anal HSIL) or
  - 2) Treatment of anal HSIL







- Screening visit: anal Pap smear and HRA with biopsies
- Study procedures:
  - All patients: Every 6 months: anal Pap, HRA
  - Active monitoring group: annual biopsies
  - Treatment group: HSIL will be treated with either imiquimod, topical 5FU, 85% TCA, IRC, electrocautery or surgery
  - \$100 per visit paid to participants
  - Study duration: 5 years



- Eligibility
  - HIV+ men and women  $\geq$  35 years with HSIL
- Outcomes
  - Development of invasive anal cancer

# Prevention

- Early diagnosis and treatment with ART
  - CDC/NCCN recommendation of universal testing
  - Risk of cancer reduced among those who indicated ART with CD4 > 500 compared to those who initiated at < 350
  - 50% reduction in NADC/ 90% reduction in KS/70% reduction in lymphoma
- Vaccination
  - HPV, HBV
- Smoking cessation
- Age appropriate screening

# HIV and Cancer

- Increased risk
- Disparities persist
- Most patients who develop cancer should be offered the same cancer therapies as HIV-negative individuals (including clinical trial participation)
- Patients should be co-managed with an oncologist and an HIV specialist